

## SEQ ID NO:1:

GGCATATTAGCTTGGGTTACTGTGAATTTTCTGACAGGTCAGCTGCATGGCCACAGA  
CAGGAGACTGTGGGGACCTTGGACCTAGGGGGAGCCTCCACCCAAATCACGTTTCCT  
GCCCCAGTTTGAGAAAACCTCTGGAACAACTCCTAGGGGGCTACCTCACTTCCTTTGA  
GATGTTTAACAGCACTTATAAGCTCTATACATAGTTACCTGGGATTTGGATTGAA  
AGCTGCAAGACTAGCAACCCTGGGAGCCCTGGAGACAGAAGGGACTGATGGGCACA  
CTTTCCGGAGTGCCTGT

## SEQ ID NO:2:

GCGGGCTGCCGCGCAAGGGTGGCGCGCGCGCGTTCCTTGTTTCCTGGTCAACAAAG  
AAATGTGGAGTGTCTTGGCTGAATCCTCATACAGACAAGATCATTATGGTGCTGTTA  
GGTTGAAAAAGTGATATAATAAAGGAACCAAGGAGAAAATTCAGAAGGAAAGAAA  
AAATTGCCTCTGCAGGTGTGCGAGCAGGATTGCTTCTGCAACAAAAGCCTCCACCCA  
GCCACATCTTGGGAAAAGAATGGCCACTTCTTGGGGCACAGTCTTTTTCATGCTGGT  
GGTATCCTGTGTTTGCAGCGCTGTCTCCACAGGAACCAGCAGACTTGGTTTGAGGG  
TATCTTCCTGTCTTCCATGTGCCCCATCAATGTCAGCGCCAGCACCTTGTATGGAATT  
ATGTTTGATGCAGGGAGCACTGGAACCTCGAATTCATGTTTACACCTTTGTGCAGAAA  
ATGCCAGGACAGCTTCCAATTCTAGAAGGGGAAGTTTTTGATTCTGTGAAGCCAGGA  
CTTTCTGCTTTTGTAGATCAACCTAAGCAGGGTGCTGAGACCGTTCAAGGGCTCTTA  
GAGGTGGCCAAAGACTCAATCCCCCGAAGTCACTGGAAAAGACCCCAAGTGGTCCT  
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TTGAGGTAAAGGAGATCTTCAGGAAGTCACCTTTCCTGGTACCAAAGGGCAGTGTTA  
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CAGGTCAGCTGCATGGCCACAGACAGGAGACTGTGGGGACCTTGGACCTAGGGGGA  
GCCTCCACCCAAATCACGTTTCCTGCCCCAGTTTGAGAAAACCTCTGGAACAACTCCT  
AGGGGGCTACCTCACTTCCTTTGAGATGTTTAACAGCACTTATAAGCTCTATACAT  
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AAGCAGAGTGGATCTTTGGGGGTGTGAAATACCAGTATGGTGGCAACCAAGAAGGG  
GAGGTGGGCTTTGAGCCCTGCTATGCCGAAGTGCTGAGGGTGGTACGAGGAAACT  
TCACCAGCCAGAGGAGGTCCAGAGAGGTTCTTCTATGCTTTCTCTTACTATTATGA  
CCGAGCTGTTGACACAGACATGATTGATTATGAAAAGGGGGGTATTTTAAAAGTTGA  
AGATTTTGAAGAAAAGCCAGGGAAGTGTTGTGATAACTTGGAAAACCTTCACCTCAG  
GCAGTCCTTTCCTGTGCATGGATCTCAGCTACATCACAGCCCTGTTAAAGGATGGCT  
TTGGCTTTGCAGACAGCACAGTCTTACAGCTCACAAAGAAAGTGAACAACATAGAG  
ACGGGGCTGGGCCTTGGGGGGCCACCTTTCACCTGTTGCAGTCTCTGGGCATCTCCCAT  
TGAGGCCACGTACTTCCTTGGAGACCTGCATTTGCCAACACCTTTTTTAAGGGGAGGA  
GAGAGCACTTAGTTTCTGAACTAGTCTGGGGACATCCTGGACTTGAGCCTAGAGATT  
WRGTTAATTAASCGGCCGAGCTTATCCTTWATRAGGTAATTTACTTGCMTGGCCGCG  
TTTACACGTCGTGATGGNAACCTGCGTCCCAACTAACGCTTGASAMATCCCCTTCG  
CAGCTGCGATACCAAAGCCGACGACGCCTTCCACAGTGCCA

Figure 1

SEQ ID NO:3.

MATSWGTVFFMLVVSCVCSAVSHRNQQTWFEGIFLSSMCPINVSASTLYGIMFDAGSTG  
TRIHVYTFVQKMPGQLPILEGEVFDSEVKPGLSAFVDQPKQGAETVQGLLEVAKDSIPRSH  
WKKTPVVLKATAGLRLLPEHKAKALLFEVKEIFRKSPFLVPKGSVSIMDGSDEGILAWV  
TVNFLTGQLHGHRQETVGTLDLGGASTQITFLPQFEKTLEQTPRGYLTSEMFNSTYKLY  
THSYLGFGGLKAARLATLGALETEGTDGHTFRSACLPRWLEAEWIFGGVKYQYGGNQEG  
EVGFEP CYAEVLRVVRGKLHQPEEVQRGSFYAFSYYYDRAVD TDMIDYEKGGILKVED  
FERKAREVCDNLENFTSGSPFLCMDLSYITALLKDGFGFADSTVLQLTKKVNNIETGWA  
LGATFHLLQSLGISH

Figure 2



1	M A T S W G T V F F M L V V S C V C S A V S E R N Q Q T W F E Q I F L S S K C P	246	prot
1	M A T S W G A V F - M L L A A Q V Q S T V F Y I R E Q Q T W F E Q I F L S S K C P	mur	ncpase
41	I N V S A S T Y G I M F D A G S T G T R I H V Y T F V Q A K R Q Q L P L L E Q	246	prot
40	I N V S A G T F Y G I M F D A G S T G T R I H V Y T F V Q K T E G Q L P L L E Q	mur	ncpase
81	E V F D S V K P G L S A F V D Q P K Q G A E T V Q Q L L E V A K D S I P R S A W	246	prot
80	E V F D S V K P G L S A F V D Q P K Q G A E T V Q I E L L E V A K D S I P R S A W	mur	ncpase
121	K K T P V V L K A T A G L R L L P E H K A K A L L E E V K E I F R K S P F L V P	246	prot
120	E R I T P V V L K A T A G L R L L P E Q K A Q A L L E V E E I F K N S P F L V P	mur	ncpase
161	K G S V S I M D G S D E G I L A W V T V N F L T G Q L H G H R Q E T V G T L D L	246	prot
50	D G S V S I M D G S Y E G I L A W V T V N F L T G Q L H G R G Q E T V G T L D L	mur	ncpase
201	G G A S T Q I T F L P Q F E K T L E Q T P R G Y L T S F E M F N S T Y K L Y T H	246	prot
200	G G A S T Q I T F L P Q F E K T L E Q T P R G Y L T S F E M F N S T F K L Y T H	mur	ncpase
241	S Y L G F G L K A A R L A T L G A L E T E G T D G H T F R S A C L P R W L E A E	246	prot
240	S Y L G F G L K A A R L A T L G A L E A K G T D G H T F R S A C L P R W L E A E	mur	ncpase
281	W I F G G V K Y Q Y G G N Q E G E V G F E P C Y A E V L R V V R G K L H Q P E E	246	prot
280	W I F G G V K Y Q Y G G N Q E G E M G F E P C Y A E V L R V V Q G K L H Q P E E	mur	ncpase
321	V Q R G S F Y A F S Y Y Y D R A V D T D M I D Y E K G G I L K V E D F E R K A R	246	prot
320	V R G S A F Y A F S Y Y Y D R A A D T H I L I D Y E K G G V L K V E D F E R K A R	mur	ncpase
361	E V C D N L E N F T S G S P F L C M D L S Y I T A L L K D G F G F A D S T V L I Q	246	prot
360	E V C D N L G S F S S G S P F L C M D L T Y I T A L L K D G L G F A E R H P L T	mur	ncpase
401	L T K K V N N I E T G W - A L G A F - - - - - H L L Q S L G I S H	246	prot
400	- A H K E S E Q H R D W L G L G G H L S P A P V S G H H Q L R P S S T S E A C I	mur	ncpase
428		246	prot
439	S E P V F S Q E G V D S E T F S D L S G K A W P E T R	mur	ncpase

Figure 4

# Apyrase Conserved Regions in CD39-L4

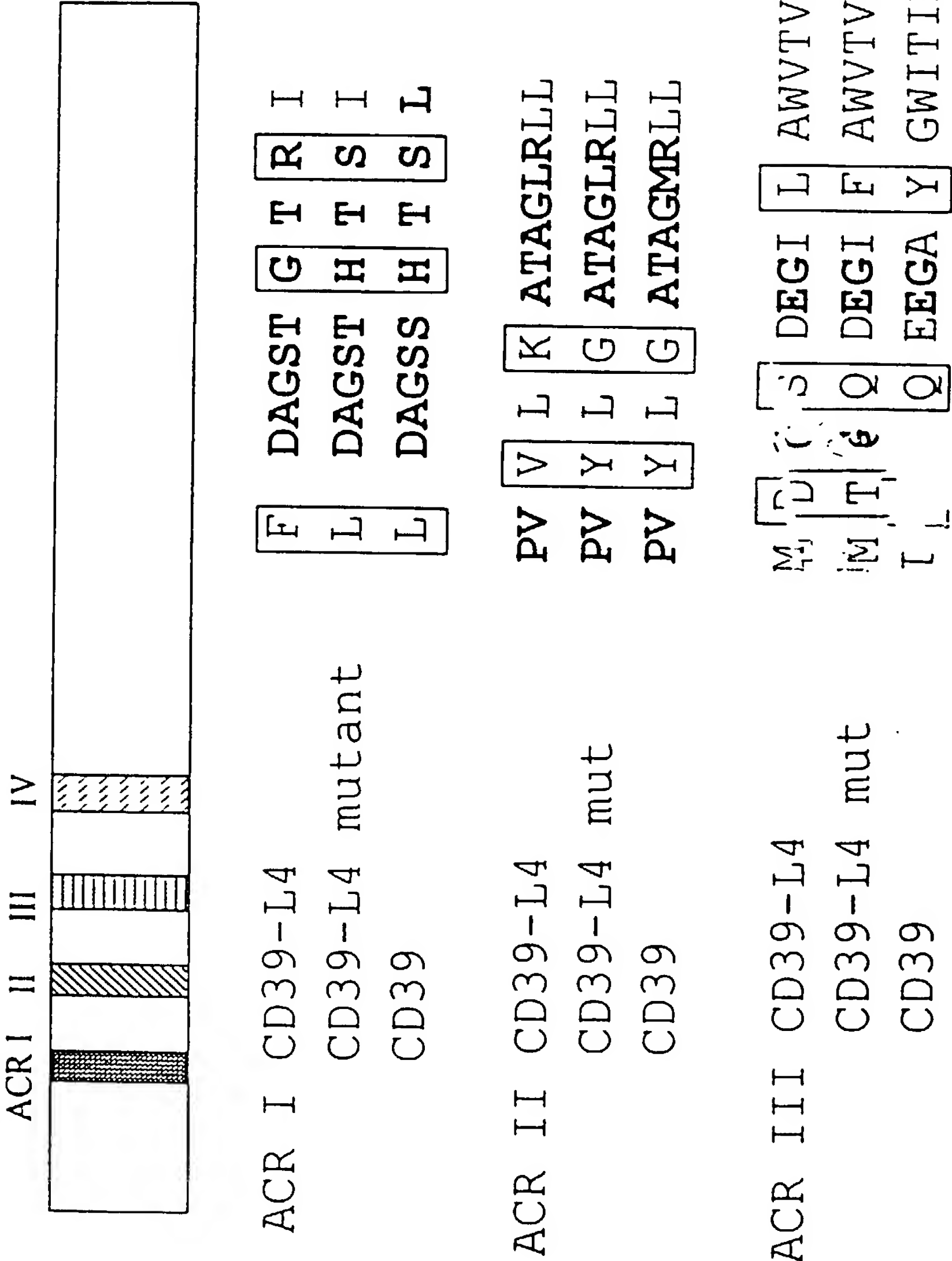


FIG. 5

1,109,204, 0,250,002

Nucleotide sequence of the CD39-L4 mutant ACRIII (SEQ ID NO:6). The nucleotide changes have been highlighted. The G to A and A to C changes at positions 502 and 503 produce a Thr, the T to C, C to A and C to A changes at positions 508-510 result in a Gln and the A to C changed at position 525 result in a Phe.

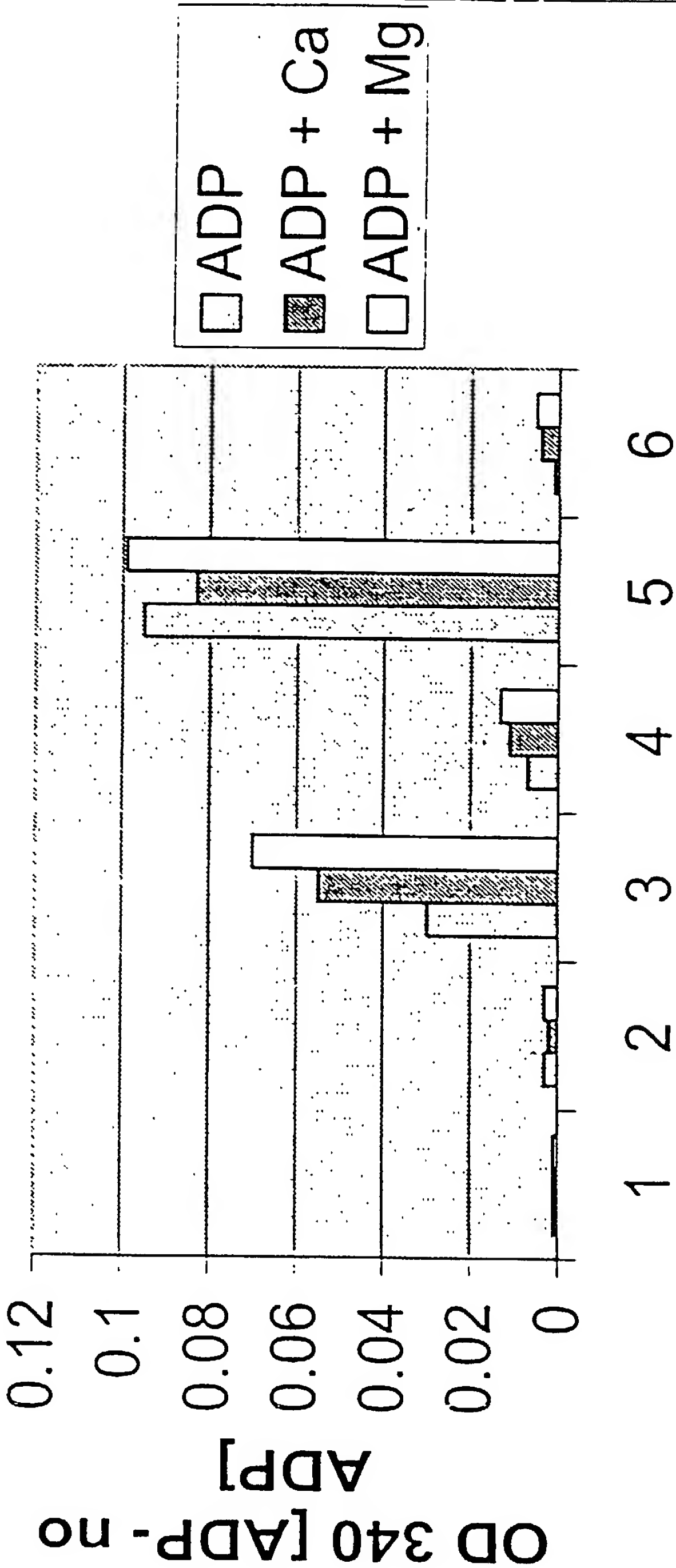
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ATGGCCACTTCTTGGGGCACAGTCTTTTTTCATGCTGGTGGTATCCTGTGTTTGCAGCGCTGTCT
CCCACAGGAACCAGCAGACTTGGTTTGAGGGTATCTTCCTGTCTTCCATGTGCCCCATCAATGT
CAGCGCCAGCACCTTGTATGGAATTATGTTTGATGCAGGGAGCACTGGAATTCGAATTCATGTT
TACACCTTTGTGTCAGAAAATGCCAGGACAGCTTCCAATTCTAGAAGGGGAAGTTTTTGATTCTG
TGAAGCCAGGACTTTCTGCTTTTGTAGATCAACCTAAGCAGGGTGCTGAGACCGTTCAAGGGCT
CTTAGAGGTGGCCAAAGACTCAATCCCCCGAAGTCACTGGAAAAAGACCCAGTGGTCTTAAAG
GCAACAGCAGGACTACGCTTACTGCCAGAACACAAAGCCAAGGCTCTGCTCTTTGAGGTAAAGG
AGATCTTCAGGAAGTCACCTTTCCTGGTACCAAAGGGCAGTGTTAGCATCATGACTGGACAAGA
CGAAGGCATATTGGCTTGGGTTACTGTGAATTTTCTGACAGGTCAGCTGCATGGCCACAGACAG
GAGACTGTGGGGACCTTGGACCTAGGGGGGAGCCTCCACCCAAATCACGTTCTGCCCCAGTTTG
AGAAAACCTCTGGAACAAACTCCTAGGGGGCTACCTCACTTCCTTTGAGATGTTTAACAGCACTTA
TAAGCTCTATACACATAGTTACCTGGGATTTGGATTGAAAGCTGCAAGACTAGCAACCTTGGGA
GCCCTGGAGACAGAAGGGACTGATGGGCACACTTTCCGGAGTGCTGTTTACCGAGATGGTTGG
AAGCAGAGTGGATCTTTGGGGGTGTGAAATACCAGTATGGTGGCAACCAAGAAGGGGAGGTGGG
CTTTGAGCCCTGCTATGCCGAAGTGCTGAGGGTGGTACGAGGAAAACCTCACCAGCCAGAGGAG
GTCCAGAGAGGTTCTTCTATGCTTTCTCTTACTATTATGACCGAGCTGTTGACACAGACATGA
TTGATTATGAAAAGGGGGGTATTTTAAAGTTGAAGATTTTGAAGAAAAGCCAGGGAAGTGTG
TGATAACTTGGAACCTTCACC TCAGGCAGTCCTTTCTGTGCATGGATCTCAGCTACATCAC
AGCCCTGTTA AAGGATGGCTTTGGCTTTGCAGACAGCACAGTCTTACAGCTCACAAAGAAAGT
GAAC AACATAG AGACGGGCTGGGCCTTGGGGGCCACCTTTCACCTGTTGCAGTCTCTGGGCA
TCTCCCATTTGA
```

Amino acid sequence of CD39-L4 mutant ACR III (SEQ ID NO:7). The amino acid changes are D to T (a.a. 168), S to Q (a.a. 170) and L to F (a.a. 175). The changes are shown in bold.

```
MATSYGTVFFMLVVSCVCSAVSHRNQQTWFEGIFLSSMCPINVSASTLYGIMFDAGSTGT
RIHVYTFVQKMPGQLPILEGEVFDVSVKPGLSAFVDQPKQGAETVQGLLEVAKDSIPRSHW
KKTPVVLKATAGLRLLPEHKAKALLFEVKEIFRKSPFLVPKGSVSIMTGQDEGIFAWVTV
NFLTGQLHGHRQETVGTLDLGASTQITFLPQFEKTLEQTPRGYLTSFEMFNSTYKLYTH
SYLGFGGLKAARLATLGALETEGTDGHTFRSACLPRWLEAEWIFGGVKYQYGGNQEGEVGF
EPCYAEVLRVVRGKLHQPEEVQRGSFYAFSYYYDRAVDTDMDYKGGILKVEDFERKAR
EVCDNLENFTSGSPFLCMDLSYITALLKDGFGFADSTVLQLTKKVNNIETGWALGATFHL
LQSLGISH
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FIG. 6

FIG. 2 ADPase activity of CD39-L4  
ACR mutants



1) ACR I; 2) ACR II; 3) ACR III; 4)  
Wild Type; 5) CD39; 6) Vector

CD39-L4

FIG. 7



10097063.030592

SEQ ID No-3	M A T S W G	- - - - -	V F F M L V V S C V C S A V S H R N Q Q T W F E G I F L S S M C P I N V S A S	46
SEQ ID No-5	M A T S W G T	- - - - -	V F F M L V V S C V C S A V S H R N Q Q T W F E G I F L S S M C P I N V S A S	46
CD39Human.seq	M E D T K E S N V K T F C S K N I L A I L G F S S I I A V I A	- - - - -	L L A V G L T Q - - N K A L P E N	46
SEQ ID No-3	T L Y G I M F D A G S T G T R I H V Y T F V Q K M P G Q L P I L E G E V F D S V K	-	P G L S A F V D Q P K Q G	100
SEQ ID No-5	T L Y G I M F D A G S T G T R I H V Y T F V Q K M P G Q L P I L E G E V F D S V K	-	P G L S A F V D Q P K Q G	100
CD39Human.seq	V K Y G I V L D A G S S H T S L Y I Y K W P A E K E N D T G V V H Q V E E C R V K	G	P G I S K F V Q K V N E I	101
SEQ ID No-3	A E T V Q G L L E V A K D S I P R S H W K K T P V V L K A T A G L R L L	- - -	P E H K A K A L L F E V K E I F	152
SEQ ID No-5	A E T V Q G L L E V A K D S I P R S H W K K T P V V L K A T A G L R L L	- - -	P E H K A K A L L F E V K E I F	152
CD39Human.seq	G I Y L T D C M E R A R E V I P R S Q H Q E T P V Y L G A T A G M R L L R M E S E	E L A D R V L D V V E R S L		156
SEQ ID No-3	R K S P F L V P K G S V S I M D G S D E G I L A W V T V N F L T G Q L	- - - - -	H G H R Q E T V	195
SEQ ID No-5	R K S P F L V P K G S V S I M D G S D E G I L A W V T V N F L T G Q L	- - - - -	H G H R Q E T V	195
CD39Human.seq	S N Y P F D F Q - - G A R I I T G Q E E G A Y G W I T I N Y L L G K F S Q K T R W F S I V P Y E T N N Q E T F			209
SEQ ID No-3	G T L D L G G A S T Q I T F L P Q F E K T L E Q T P R G Y L T S F E M F N S T Y K L Y T H S Y L G F G L K A A			250
SEQ ID No-5	G T L D L G G A S T Q I T F L P Q F E K T L E Q T P R G Y L T S F E M F N S T Y K L Y T H S Y L G F G L K A A			250
CD39Human.seq	G A L D L G G A S T Q V T F V P Q - N Q T I E S P D N A - - L Q F R L Y G K D Y N V Y T H S F L C Y G K D Q A			261
SEQ ID No-3	- - - R L A T L G A L E T E G	- - - - -	T D G H T F R S A C L P R W L E A E W I F G G V K	287
SEQ ID No-5	- - - R L A T L G A L E T E G	- - - - -	T D G H T F R S A C L P R W L E A E W I F G G V K	287
CD39Human.seq	L W Q K L A K D I Q V A S N E I L R D P C F H P G Y K K V V N V S D L Y K T P C T K R - F E M T L P F Q Q F			314
SEQ ID No-3	Y Q Y G G N Q E G E V G F E P C Y A E V L R V V R G K	- - - - -	L H Q P E E V Q R G S F Y A F S	330
SEQ ID No-5	Y Q Y G G N Q E G E V G F E P C Y A E V L R V V R G K	- - - - -	L H Q P E E V Q R G S F Y A F S	330
CD39Human.seq	- - - - - E I Q G I G N Y Q Q C H Q S I L E L F N T S Y C P Y S Q C A F N G I F L P P L Q G D F G A F S A F			363
SEQ ID No-3	Y Y Y D R	- - -	A V D T D M I D Y E K G G I L K V E D F E R K A R E V C D N L E N F T S G S P	378
SEQ ID No-5	Y Y Y D R	- - -	A V D T D M I D Y E K G G I L K V E D F E R K A R E V C D N L E N F T S G S P	378
CD39Human.seq	- Y F V M K F L N L T S E K V S Q E K V T E M - M K K E C A Q P W E	- - -	E I K T S Y A G V K E K Y L S E Y C F	414
SEQ ID No-3	D L S Y I T A L L K D G F G F A D S T	- - - - -	V L Q L T K K V N N I E T G W	412
SEQ ID No-5	D L S Y I T A L L K D G F G F A D S T	- - - - -	V L Q L T K K V N N I E T G W	412
CD39Human.seq	S G T Y I L S L L L Q G Y H F T A D S W E H I H F I G K I Q G S D A G W T L G Y M L N L T			459
SEQ ID No-3	A L G A T F H L L Q S L G I S H			428
SEQ ID No-5	- - - - - V L R			406
CD39Human.seq	- - - - - N M I P A E Q P L S T P L S H S T Y V F L M V L F S L V L F T V A I G I L I F H Y P			502



10092043.030507

mur ntpase	M A T S W G A	- M L I I A C V G S T V F Y R E Q Q T W F E G V F L S S M C P I N V	G T F Y G I M F D A	54
SEQ ID No-3	M A T S W G T	- F M L V V S C V C S A V S H R N Q Q T W F E G I F L S S M C P I N V	. S T L Y G I M F D A	55
SEQ ID No-5	M A T S W G T V F F M L V V S C V C S A V S H R N Q Q T W F E G I F L S S M C P I N V S A S T L Y G I M F D A			55
mur ntpase	G S T G T R I H V Y T F V Q K T A G Q L P F L E G E I F D S V K P G L S A F V D Q P K Q G A E T V Q E L L E V			109
SEQ ID No-3	G S T G T R I H V Y T F V Q K M P G Q L P I L E G E V F D S V K P G L S A F V D Q P K Q G A E T V Q G L L E V			110
SEQ ID No-5	G S T G T R I H V Y T F V Q K M P G Q L P I L E G E V F D S V K P G L S A F V D Q P K Q G A E T V Q G L L E V			110
mur ntpase	A K D S I P R S H W E R T P V V L K A T A G L R L L P E Q K A Q A L L L E V E I F K N S P F L V P D G S V S			164
SEQ ID No-3	A K D S I P R S H W K K T P V V L K A T A G L R L L P E H K A K A L L F E V K E I F R K S P F L V P K G S V S			165
SEQ ID No-5	A K D S I P R S H W K K T P V V L K A T A G L R L L P E H K A K A L L F E V K E I F R K S P F L V P K G S V S			165
mur ntpase	I M D G S Y E G I L A W V T V N F L T G Q L H G R G Q E T V G T L D L G G A S T Q I T F L P Q F F E K T L E Q T			219
SEQ ID No-3	I M D G S D E G I L A W V T V N F L T G Q L H G H R Q E T V G T L D L G G A S T Q I T F L P Q F F E K T L E Q T			220
SEQ ID No-5	I M D G S D E G I L A W V T V N F L T G Q L H G H R Q E T V G T L D L G G A S T Q I T F L P Q F F E K T L E Q T			220
mur ntpase	P R G Y L T S F E M F N S T F K L Y T H S Y L G F G L K A A R L A T L G A L E A K G T D G H T F R S A C L P R			274
SEQ ID No-3	P R G Y L T S F E M F N S T Y K L Y T H S Y L G F G L K A A R L A T L G A L E T E G T D G H T F R S A C L P R			275
SEQ ID No-5	P R G Y L T S F E M F N S T Y K L Y T H S Y L G F G L K A A R L A T L G A L E T E G T D G H T F R S A C L P R			275
mur ntpase	W L E A E W I F G G V K Y Q Y G G N Q E G E M G F E P C Y A E V L R V V Q G K L H Q P E E V R G S A F Y A F S			329
SEQ ID No-3	W L E A E W I F G G V K Y Q Y G G N Q E G E V G F E P C Y A E V L R V V R G K L H Q P E E V Q R G S F Y A F S			330
SEQ ID No-5	W L E A E W I F G G V K Y Q Y G G N Q E G E V G F E P C Y A E V L R V V R G K L H Q P E E V Q R G S F Y A F S			330
mur ntpase	Y Y Y D R A A D T H L I D Y E K G G V L K V E D F E R K A R E V C D N L G S F S S G S P F L C M D L T Y I T A			384
SEQ ID No-3	Y Y Y D R A V D T D M I D Y E K G G I L K V E D F E R K A R E V C D N L E N F T S G S P F L C M D L S Y I T A			385
SEQ ID No-5	Y Y Y D R A V D T D M I D Y E K G G I L K V E D F E R K A R E V C D N L E N F T S G S P F L C M D L S Y I T A			385
mur ntpase	L L K D G L G F A E R H P L T - A H K E S E Q H R D W L G L G G H L S P A P V S G H Q L R P S S T S E A C I			438
SEQ ID No-3	L L K D G F G F A D S T V L Q L T K K V N N I E T G W - A L G A T F - - - - - H L L Q S L G I S - - - - -			427
SEQ ID No-5	L L K D G F G F A D S T V L Q - A - - - - - - - - - - - - - - - A V L R - - - - -			405
mur ntpase	S E P V F S Q E G V D S E T F S D L S G K A W P E T R			465
SEQ ID No-3	- H			428
SEQ ID No-5	- -			406

FIG 9